Disorders of lipid metabolism (detailed)

Lipid transport disorders

The classification of hyperlipoproteinemias was based in the past mainly on the "Fredrickson's electrophoretic scheme", which allowed the hyperlipoproteinemia to be divided into six groups marked with Roman numerals I to V, with type II having subgroups IIa and IIb. This classification is currently being withdrawn. Fredrickson's lipoprotein type is not a nosological entity; in the same individual, it may vary depending on lifestyle or medication (eg type V may switch to type IV and then type IIb). Similarly, a genetically well-defined disease may manifest as a different lipoprotein type in different individuals (e.g., familial combined hyperlipidemia may manifest as electrophoretic type IIb, but also as type IV or IIa).

Fredrickson's classification of hyperlipoproteinemias

Type	Occurrence (% of total hyperlipoproteinemias)	ELFO (multiplied fraction)	Cholesterol	TAG	Serum appearance	Risk of atherosclerosis
I	1 %	chylomicron	slightly increased	much increased	creamy	low
IIa	10–15 %	(LDL)	much increased	normal	clear	considerably high
IIb	22–25 %	VLDL, LDL	increased	slightly above the norm	opalescent	considerably high
III	1–5 %	LDL, VLDL atypical	increased	increased	cloudy	considerably high
IV	50–60 %	VLDL	slightly increased	slightly above the norm	cloudy	high
V	1–5 %	VLDL + chylomicron	values between type III and IV	much increased	creamy	low

Apolipoproteins in disorders of lipoprotein metabolism

Syndrome	A-I	A-II	B	C-I	C-II	C-III	D	E	
Exogenous hyperlipidemia (type I) (chylomicrons)	↓↓↓	↓↓↓	↓	-	-	N	N	-	lipoprotein lipase deficiency
Hypercholesterolemia (type IIa) (LDL)	N	N	↑↑	N	N	N	N	N	increase of free LP-B
Combined hyperlipidemia (type IIb) (LDL+VLDL)	N	N	↑↑	N	N	↑↑	N	N	increase of the complex LP-B:C
Remnant-hyperlipidemia (familiar dysbetalipoproteinemia)	N	N	N	↑	↑	↑	N	↑↑	defect apoE-3 a E-4, increase of the complex LP-B: C: E-1 a 2
Endogenous hyperlipidemia (type IV) (VLDL)	N	N	↑	N	N	↑↑	N	N	
Mixed hyperlipidemia (type V), (VLDL+chylomicrons)	N	N	↑	↑↑↑	↑↑↑	↑↑	N	↑↑	increase of the complex LP-B: C: E
Analfalipoproteinemia (Tangier disease)	missing	↓↓↓	N-↓	↓	N	↓	↓↓	N-↓	
Abetalipoproteinemia	↓↓	↓↓	missing	↓	↓↓	↓↓↓	↓	N	
Hypobetalipoproteinemia	N	N	↓↓↓	N	N	↓	-	N	
Lecithin deficiency: cholesterol acyl transferase (lamellar hyperlipoproteinemia)	↓↓	↓↓	↓	-	-	-	N	-	

The current classification of primary hyperlipoproteinemias and hypolipoproteinemias is based on the underlying etiopathogenetic cause based on genetic changes.

Hyperlipoproteinemia

Primary hypercholesterolemia

Primary Hypercholesterolemia

Primary mixed hyperlipidemia

Primary mixed hyperlipidemia

It is the most common genetic disorder of lipoprotein metabolism . The frequency is estimated at 1: 100 to 1:50. Heredity is usually marked as autosomal recessive.

Clinical manifestations

It often occurs in obese and diabetics . There are no xanthomas or arcus corneae; pathological manifestations of atherosklerosis (coronary heart disease, lower limb ischemia) do not begin until adulthood.

Biochemical findings

An abnormal lipid finding is usually not detected until adulthood. The serum is clear or opalescent. VLDL (pre-β-lipoproteins), also LDL (β-lipoproteins) and apoprotein B are elevated, [cholesterol]] is between 10-15 mmol / l, triacylglycerols are between 2.26-5.65 mmol / l. HDL-cholesterol and apoprotein C-II and C-III are usually reduced. Lipoprotein electrophoresis shows familial combined hyperlipoproteinemia such as type IIb, IV or even IIa or V. Sometimes another fraction of pre-α (pre-α1 and pre-α2) is evident, caused by an increase in lipoprotein (a) [Lp (a)]. Chylomicrons are not detected on an empty stomach.

Pathobiochemistry

The cause is thought to be an abnormally high synthesis of Apo B in the liver, accompanied by increased VLDL production.

Prognosis

A common complication is myocardial infarction before the age of 60; an association with diabetes and obesity is common.

Healing

- Above all, lifestyle modification: weight reduction, diet with lower fat content (preference for fat with unsaturated fatty acids instead of saturated ones) - reduction of cholesterol intake.
- Drug therapy only in patients for whom lifestyle modification has not been shown to be helpful; fibrates, are most often used , ev.resins, (e.g. Lipanthyl® or Gevilon® in combination with Colestide®); sometimes nicotic acid helps.

Familial dysbetalipoproteinemia (ie type III hyperlipoproteinemia, increase in β-VLDL)

Dysbetalipoproteinemia (type III hyperlipidemia) is a rare inherited disorder characterized by a defect in the removal of chylomicron and VLDL residues. The underlying disorder is homozygosity for the mutant form of apo E (apo E 2), which binds poorly to liver receptors. As a result, chylomicron residues accumulate as well as cholesterol-rich VLDL (β-VLDL)[1].

Clinical manifestations

- Various forms of xanthomas dominate :
  - tuberous xanthomas (in 80%),
  - palmar xanthomas (70%) - are characteristic,
  - tendon xanthomas (30%),
  - eruptive xanthomas (rare).
- Hyperuricaemia and diabetes are observed in about half of patients.
- Early atherosclerotic changes first affect the lower limbs and coronary arteries (in men before the age of 40, in women before the age of 50).

Biochemical findings

Opalescent serum; increased both cholesterol and triacylglycerols: S-cholesterol usually above 7.5 mmol / l, sometimes up to 25 mmol / l, S-triacylglycerols 2-10 mmol / l, rarely 20 mmol / l.

Characteristic appearance of ELFO-lipoproteins: "broad" β-fraction (merging pre-β and β fractions). There is an abnormal fraction between VLDL and LDL (so-called β-VLDL) on the polyacrylamide gel. An increase in the cholesterol / triacylglycerol ratio to> 0.30, a decrease in HDL and LDL cholesterol and, conversely, an increase in VLDL, IDL and chylomicron residues are characteristic.

Primary hypertriacylglycerolemia

Familial hyperchylomicronemia (= familial hyperlipoproteinemia type I)

This rare disease with autosomal recessive inheritance is caused by the lack of the enzyme lipoprotein lipase (LPL). The defect of the LPL protein cofactor (apoprotein C-II) or the presence of an LPL inhibitor also belongs to the same group. Clinical signs

- abdominal pain (75% of cases) located in the epigastrium around the navel, sometimes shooting into the back,
- hepatosplenomegaly (66%),
- eruptive xanthomas (50%) with yellowish skin nodules,
- retinal lipemia: the milky appearance of blood vessels on the back of the eye.

Biochemical findings: Milky or creamy appearance of serum due to persistent chylomicronemia. (even on an empty stomach). When standing in a refrigerator (4 ° C) overnight, a layer of floating chylomicrons forms on the surface. Triacylglycerol values often over 20 mmol / l (sometimes up to 120 mmol / l); decrease in HDL- and LDL-cholesterol,

as well as apoproteins A-I, A-II, B and D. The LDL-cholesterol / phospholipids ratio, is reduced, as do HDL-cholesterol / phospholipids. The post-heparin lipolytic activity test shows zero or very low activity.

Pathobiochemistry: Lack of lipoprotein lipase causes the accumulation of chylomicrons that cannot be normally degraded and which are removed unnaturally by macrophages. In the apo C-II defect, LPL is present but not active.

Prognosis: There is no increased risk of atherosclerosis, but there is a significant risk of acute pancreatitis (especially in hypertriacylglycerolemia above 20 mmol / l).

Healing:

- Strict dietary fat restriction, for adults below 30 g / d (preferably 15 g / d), in the form of vegetable fat rich in polyenoic fatty acids.
- Supply of fat-soluble vitamins.
- Administration of fats with medium-chain fatty acids (C8 – C12). They are absorbed into the portal circulation directly.
- Drug treatment with hypolipids fails; fibrates are even contraindicated (inhibit even residual LPL activity).

Familial hypertriacylglycerolemia (= type IV = increase in VLDL)

It is a familial hypertriacylglycerolemia in a monogenic form inherited by an autosomal dominant. It manifests itself only in adulthood and is a common form of hyperlipoproteinemia: (0.2-0.3% of the population).

Clinical signs: The absence of tendon xanthomas is characteristic; however, there is weakness, drowsiness, indigestion, often obesity and an abnormal glucose tolerance test. The risk of coronary heart disease is not high (about twofold) unless other atherogenic factors are present (hypertension, smoking, etc.); however, there is an increased risk of ischemic lower limb disease

Biochemical findings: increase in S-triacylglycerols, often over 10 mmol / l; but the values fluctuate according to the previous diet (2.3-11.3 mmol / l). In most cases, the serum is opalescent (to increase VLDL), rarely milky (increased chylomicrons). A slight increase in S-cholesterol is usually only in cases where the level of S-triacylglycerols exceeds 3 mmol / l. However, the ratio of triacylglycerols to cholesterol is always greater than 2.5. There is an increase in pre-lipoprotein ("hyper-VLDL-emia") on electrophoresis. Apoprotein B and A levels are normal; however, apoprotein C-III is elevated. Hyperuricaemia and type 2 (non-insulin-dependent) diabetes are often associated with hyperinsulinemia. (in hyperglycemia, there is also increased glycation of ApoB, which thus acquires greater atherogenicity)

Pathobiochemistry: Increased VLDL can theoretically arise from the following causes:

- increase in VLDL synthesis in the liver,
- reduction of intravascular catabolism of VLDL.

An example of increased VLDL synthesis is hypertriacylglycerolemia induced by chronic alcohol consumption. This is because alcohol is oxidized preferentially by the liver (over other substrates such as fatty acids or glucose). Acyl-CoA accumulates, which is metabolized to triacylglycerols and their transport form: VLDL. Hyperinsulinemia also stimulates VLDL synthesis. Decreased VLDL catabolism is the second possible cause of hypertriacylglycerolemia. This disorder may be due to an excess of apoprotein C-III, which is an inhibitor of lipoprotein lipase, or a deficiency of apoprotein C-II, which in turn is an activator of LPL.

The atherogenic risk of elevated VLDL is debatable. Normal VLDLs have too large a molecule to penetrate the vascular endothelium. But the concomitant presence of other risk factors, such as hypertension and nicotinism, leads to damage to the vessel wall, and thus an atherogenic effect can occur. A change in particle size ("small VLDL") is also expected. Some authors believe that a decrease in plasma HDL reduces the reverse transport of cholesterol from peripheral cells to the liver.

Prognosis and Treatment: Treatment consists mainly in reducing ev. overweight, in a low-carb diet and a ban on alcohol.

It is recommended to use a fish oil preparation, ev. nicotinic acid; fibrates are also useful.

Familial hyperlipoproteinemia type V (= increase in VLDL + chylomicrons)

It is a relatively rare disease (1: 5,000); more often, adults who are obese have hyperuricemia and diabetes. Alcohol and estrogen use, as well as renal insufficiency, may be a causative factor.

Clinical manifestations: Type V is not atherogenic; however, there is a significant tendency for acute pancreatitis. It is associated with eruptive xanthomas, arthritis, dry eyes and mouth, and emotional lability.

Biochemical findings: Milky turbid serum for the presence of chylomicrons and VLDL. At ELFO increased pre-ß fractions and increased fraction "at the start" (chylomicrons). S-triacylglycerols range between 10-20 mmol / l (although even higher values have been reported). S-cholesterol is also elevated (especially when triacylglycerols are high). Usual values are 7.75-13 mmol / l. The VLDL-cholesterol / triacylglycerol ratio is less than 0.30 (difference from type III). As with type IV, apoprotein C-III is increased and the C-II / C-III ratio is decreased. Type V is sometimes associated with the occurrence of the unusual isoform apoE-4.

Pathobiochemistry: The cause of this type is not fully explained. It is thought to be a disorder of VLDL and chylomicron metabolism. However, postheparin lipase activity is normal (unlike type I). The reason for the simultaneous increase in VLDL and chylomicrons is explained in three possible ways: (1) Increased VLDL formation and secretion by the liver leads to saturation of the triacylglycerol-rich particle removal mechanism, (2) Triacylglycerol synthesis is normal but upturned (3) It can be a combination of both mechanisms. Alcohol-related forms are very common in some countries (eg France). Distinguishing type IV from V is difficult, as is distinguishing from the secondary form induced by diet (excessive intake of fats and carbohydrates).

Prognosis and treatment: Acute pancreatitis is uncommon. The basic treatment consists of a low-energy diet and a ban on alcohol consumption.

Hyperalphalipoproteinemia

Familial hyper-α-lipoproteinemia

It is a genetic lipoprotein abnormality associated with the occurrence of longevity in the family (8-12 years compared to the average in the population); the presumed form of heredity is autosomal dominant. However, the familial form must be distinguished from the acquired (secondary) form, e.g. in alcohol abuse or the use of contraceptives or oestrogens.

The syndrome is characterized by a marked increase in HDL-cholesterol (increase in 1-lipoprotein per ELFO), a mild to moderate increase in total plasma cholesterol, and normal concentrations of S-triacylglycerols. HDL particles containing only ApoAI are multiplied, not particles containing both ApoAI and ApoAII [LpA I: A II]. The abnormality is probably due to increased apo AI synthesis. The risk of atherosclerosis-induced cardiovascular disease is reduced.

Hypolipoproteinemia

Familial hypo-α-lipoproteinemia

It is still considered a rare genetic abnormality, probably with autosomal dominant inheritance. Plasma LDL cholesterol levels are reduced below the 5 percentile limit of the normal range. Like hyperlipoproteinemia, this anomaly is associated with longevity, probably due to the low incidence of myocardial infarction.

The biochemical finding lies in low LDL-cholesterol levels; However, the LDL fraction is always present, unlike abetalipoproteinemia, where it is completely absent. The concentration of VLDL and HDL particles can be decreased or normal or even increased. The defect consists of reduced particle formation with ApoB (about half); however, LDL catabolism is normal. Because LDL particles are a product of VLDL and patients with hypo-β-lipoproteinemia have low levels of S-triacylglycerols, VLDL production is also reduced in some individuals. the LDL receptors of the respective cells are taken up very rapidly from the plasma.

Abetalipoproteinemia

It is a rare autosomal recessively transmitted disease that completely lacks ApoB-containing lipoprotein particles. Heterozygotes have no obvious clinical signs. LDL-cholesterol levels are reduced, but otherwise, laboratory tests are normal. In contrast, homozygotes have suffered from fat malabsorption since infancy; they have steatorrhoea if their diet contains fat. They do not gain weight and have delayed growth. If they do not receive vitamin E supplementation (water-soluble preparations), progressive CNS degeneration occurs. Lack of vitamin A and carotene leads to reduced visual acuity and night blindness. Erythrocytes of a special shape appear in the blood picture, so-called acanthocytes according to horny or spur-like protrusions. They have a prolonged prothrombin time for vitamin K deficiency.

A biochemical defect is the inability to synthesize or secrete ApoB-containing lipoprotein particles. It is therefore absent in the circulation of the chylomicron; the transport of endogenous cholesterol to peripheral cells via the LDL is disrupted. Adrenal cortisol production is impaired during ACTH stimulation. Cholesterol in ApoE-containing particles is transported normally.

Hypoalphalipoproteinemia

Conditions with reduced HDL-cholesterol have an increased risk of atherosclerosis and consequent cardiovascular disease. The familial form seems to have a dominant inheritance. Abnormalities in the apoA-I polypeptide composition have also been described, and one such lipoprotein has been named according to the site of the described case of apoA-IMilano. Patients are mostly asymptomatic. Without apoA-I, HDL cannot form and without HDL, apoC-II cannot be transported back to the liver during VLDL degradation. The result is a relative deficiency of apoC-II and elevated VLDL levels.

Fisheye disease

The disease is characterized by corneal opacity. HDL-cholesterol levels are reduced to 10% of normal levels; HDL2, in particular, is reduced, while apoA-I is reduced. There is usually a higher triacylglycerolemia.

Analphalipoproteinemia (Tangier disease)

It is a rare disease with autosomal recessive inheritance, characterized by a complete lack of plasma HDL. Homozygotes have undetectable levels of HDL-cholesterol and extremely low apoA-I and apoA-II. Beta-fractions are missing from lipoprotein electrophoresis. Both total cholesterol and LDL-cholesterol are reduced; is mild hypertriacylglycerolemia. The biochemical defect probably lies in the abnormally rapid catabolism of HDL and apoA-I.

The clinical picture shows striking yellow-orange cholesterol ester deposits on the pharyngeal and rectal mucosa, enlargement of tonsils and adenoid vegetation. Patients suffer from recurrent peripheral neuropathy; they have eyelid ptosis, muscular atrophy and weak muscular reflexes. Splenomegaly and thrombocytopenia are common.

Atherosclerosis

The first step in the pathogenesis of atherosclerosis is probably damage to the endothelial cells to which monocytes and T-lymphocytes adhere; they then penetrate the intima space, where they transform into macrophages, which are the main cells involved in the atherosclerosis process. The next step is the uptake of lipoprotein particles by macrophages, mainly VLDL (IDL, particles with a high content of triacylglycerols), less so LDL; however, after free radical lipoperoxidation, LDL uptake is accelerated. This is done by means of so-called scavenger receptors, the amount of which on the cell surface is not regulated according to the need for cholesterol in the cells, as is the case with the LDL receptors described by Brown and Goldstein. This causes a massive accumulation of lipoprotein particles within the macrophages and their transformation into foam cells, which underlie the atheroma plaques. Recognition of oxidized LDL by macrophage sweeping receptors is associated with loss of lysine residues in Apo B100 ev. also with a bond with malondialdehyde and further with a covalent bond of free NH2-groups with carbonyl groups formed by lipoperoxidation. Oxidized LDL and phosphatidylcholine stimulate smooth muscle, endothelial and monocyte cells to produce chemotactic and growth factors such as PDGF (= platelet-derived growth factor), FGF (fibroblast growth factor) IL1 and TNF, and heparin-binding epidermal growth factor. This results in increased replication of smooth muscle cells, which accelerates the process of atherogenesis: endothelial cells induce the production of tissue factor by the action of oxidized LDL and reduce the synthesis of a plasminogen activator inhibitor. This provides the conditions for accelerated platelet aggregation and thrombus formation, especially at the site where the calcified (by some oxysterols) atheroma plaque ruptures.

According to current opinions, more and more importance is attached to oxidative stress. This can be used both for modulation and for mediating the effect of risk factors. According to some authors, the connecting link between causal risk factors and atherosclerosis is vascular endothelial dysfunction. Localized or generalized endothelial dysfunction is associated with a tendency to vasoconstriction, thrombogenesis, and increased vascular wall permeability to lipoprotein particles. It is often associated with reduced local synthesis and concentration of nitric oxide radicals and the weakening of its antiproliferative effect.

Lipoperoxidation is a sequence of reactions in which free oxygen and nitrogen radicals remove hydrogen from a polyunsaturated fatty acid (PUFA) molecule, changing the pentadiene arrangement of double bonds to conjugated dienes. These react with atomic oxygen (1O2) or an oxygen radical (• O2) to form a peroxyl radicals, which can attack other PUFA chains. It removes hydrogen atoms from them to form lipid hydroperoxides (lipoperoxides), cyclic peroxides and cyclic endoperoxides. Their hydrolysis produces toxic aldehydes - such as malondialdehyde (MDA), 4-hydroxy-2,3-trans-nonenal, alkoxy radicals and low molecular weight volatile hydrocarbons (pentane, hexane). One molecule of hydroxyperoxyl radical can attack a number of PUFA molecules. Termination occurs by the reaction of two radicals or by reactions with scavengers. Toxic radicals then react with the -SH and -NH2 groups in proteins, changing their chemical structure and function. Fragmentation of apoB100 occurs, and cross-linking of apo AI reduces their ability to absorb cholesterol and activate LCAT. The oxidability of LDL is affected by the amount and type of fatty acids that are part of phospholipids and cholesteryl esters. Oleic acid has an antioxidant effect; on the contrary, PUFAs of the n.3 and a-6 series have a prooxidizing character, as do trans-monoenoic fatty acids (especially elaidic acid), which result from the partial hydrogenation of vegetable and animal fats. Not only LDL but also VLDL with a high content of triacylglycerols (Sf 400) and their remnant particles are subject to oxidative modification. Intracellular transport of VLDL and VLDL remnants to macrophages via the B1 scavenger receptor (SR-B1) is significantly enhanced by their oxidative modification.

To date, more than 200 risk factors for cardiovascular disease have been identified. The 3 best known include (1) Abnormal lipids (more than 15 types of cholesterol-containing lipoproteins and 4 different types of triacylglycerol-rich particles are known; some are atherogenic), (2) high blood pressure, and (3) cigarette smoking. This is approached by others, such as diabetes, overweight, lack of physical activity and many others, including abnormalities in factors involved in blood clotting (fibrinogen, factor VII, plasminogen activator inhibitors or newly identified ones (homocysteine, isoforms apo E 4)). About 50% of myocardial infarctions result in a reduction in the normal ventricular ejection fraction, in which 75% to 95% of the stenosis is removed. in the artery, it adjusts the ejection fraction to normal in a quarter of patients and improves it in a third. When cholesterol levels can be reduced within 3-5 years, stenosis can be remodelled and reduced, improving coronary flow in many patients. angioplasty or coronary "by-pass" saves the "hibernating" myocardium, but it does not prevent later heart attacks, which occur in about half of patients as new fat deposits form in the coronary arteries. These lipid deposits are covered only by a thin layer of endothelial cells and thus represent a very unstable lesion that can easily rupture and cause massive thrombosis in the collateral-free area. This risk can be reduced by very aggressive hypolipidemic therapy.

Characteristics of the general assessment of lipid risk factors

Cholesterol

It is well known that the incidence of cardiovascular disease positively correlates between total cholesterol levels and age. It is twice as high in men and women over the age of 70 as it is in their 50s: An independent statistically significant correlation with cholesterolemia and coronary heart disease was found in the Framingham study. However, in the large group examined (with cholesterol values between 3.9 and 7.8 mmol / l) there was an overlap between the two groups (with and without coronary heart disease). The study showed that only cholesterol testing to predict risk in 90% of individuals is uncertain. As many as 20% of individuals with cholesterol below 5.2 mmol / l had coronary heart disease. According to this study, most patients with coronary heart disease had a cholesterol level of 5.8 mmol / l, individuals with values between 3.8 and 5.2 had coronary heart disease in 20%, with values between 5.2 and 7.8 in 40% and with values above 7 .8 mmol / l in 90%. It is therefore important to detect that 20% who are candidates for coronary heart disease, even though they have cholesterol of 5.2 mmol / l as well as 40% with values around 5.8 mmol / l. The values of HDL-cholesterol, LDL-cholesterol and triacylglycerols are discriminatory parameters.

High-Density Lipoproteins (HDL)

High levels of HDL-cholesterol (HDL-C) are associated with a low risk of coronary heart disease and, conversely, individuals who have total cholesterol <5.2 mmol / l but HDL-C <1. 04 mmol / l have the same high risk of coronary heart disease as individuals with cholesterol 6.7 mmol / l. Individuals with cholesterolemia of 6.7 mmol / l are not protected by HDL-C levels of 1.3–1.5 mmol / l. It follows that there is a different optimal adequate HDL-C level that corresponds to a certain cholesterol level. For simplicity, it is recommended to calculate the total ratio. chol. / HDL-C, which has better risk prediction, especially in the elderly, than the values of both parameters alone. Using the index total. cholesterol / HDL-C can be predicted in up to 80% of individuals ev. restenosis after treatment based on coronary angioplasty. Restenosis usually occurs within 6 months after the procedure. Intensive hypolipidemic therapy lasting at least one year may improve the situation.

Low-Density Lipoproteins (LDL)

LDL-cholesterol is a very important risk factor, but in itself, if its level is not enormously high (> 7.8 mmol / l), it has no general value in predicting individual risk. Studies have shown that e.g. the peak incidence of coronary heart disease (ie 40%) is at a cholesterol level of 5.8 mmol / l. To identify the risk, it is necessary to examine the level of HDL-cholesterol.

Triacylglycerols (= TG)

Plasma triacylglycerol levels are another independent risk factor for coronary heart disease, especially HDL-C. Men with TG levels> 1.7 mmol / l and HDL-C <1.04 mmol / l have a double risk. Women with TG> 1.7 mmol / l and HDL-C <1.35 mmol / l have a high risk of coronary heart disease. Increased insulin resistance, hypertension and central obesity, and a tendency to hyperuricemia were also found in these individuals. Reaven called this group metabolic syndrome X. Another study (PROCAM) found that in 73 individuals with newly developed coronary heart disease, 37 had TG> 1.7 mmol / l and HDL-C <0.9 mmol / l. In the Helsinki Heart Study, treatment with gemfibrozil in patients with LDL / HDL> 5 and TG> 2.3 mmol / l decreased the incidence of myocardial infarction by 71%.

Very Low-Density Lipoproteins (VLDL)

The liver is made up of different types of VLDL. Individuals on a vegetarian diet or with higher alcohol consumption, as well as patients treated with estrogens or colestipol, produce so-called "puffy" VLDL (ie larger, non-atherogenic VLDL by Sf = 60-400). Most of these particles return from the circulation back to the liver or are transformed into LDL-A particles, which are taken up only by small amounts by macrophages; most return to the liver. In contrast, in individuals living on a diet rich in (saturated) fatty acids and cholesterol, which leads to a central type of obesity, producing small VLDL of increased density (Sf = 12–60), which are metabolized to small dense LDL-B. Both of these lipoprotein particles are eagerly taken up by macrophages in the artery wall. TG levels are considered a suitable marker of this situation (70% of cases with hypertriacylglycerolemia have elevated small dense VLDL, which are highly atherogenic). It has been found that when the TG level rises to 1.1 mmol / l, small dense LDL-B particles begin to appear; at a TG concentration of about 1.7 mmol / l, even normal (non-atherogenic) LDL A particles disappear completely from the circulation and only atherogenic LDL-B particles remain in the plasma. Conclusion: In order to detect a higher risk, it is necessary to first examine the whole. cholesterol; if> 3.8 mmol / l and the index total. chol. / HDL-C> 4, it is necessary to examine TG (if not> 1.7 mmol / l) or LDL to determine whether hypertriacylglycerolemia (fibrates, niacin) or elevated cholesterol (statins) should be treated.

Investigation of individual risk factors for atherosclerosis

Lipoproteins

Apolipoprotein AI (low value)

It is a structural protein mainly of HDL particles and also an activator of LCAT. Low values are a risk factor for coronary heart disease. Physiological values:

- men: 1.0–1.5 g / l
- women: 1.1-1.6 g / l

A value below 0.9 g / l is risky

Apolipoprotein B

Physiological values (adults):

- men: 1.05 ± 0.25 g / l
- women: 0.95 ± 0.25 g / l

Tab. 3: Evaluation of apoB in relation to the risk of atherosclerosis

value	Risk
up to 0,9 g/l	very low
0,9–1,20 g/l	low
1,20–1,40 g/l	medium
over 1,40 g/l	high

Apolipoprotein E, isoforms

ApoE is a major component of VLDL and chylomicron residues. The apoE gene located on chromosome 19 has 3 alleles (apoE-2, apoE-3, apoE-4), which give rise to six possible variants (3 homozygous, 3 heterozygous). The difference between the individual isoforms is due to the exchange of cysteine for arginine in the polypeptide chain; apoE-2 has 2 cysteine residues, apoE3 1 cysteine and 1 arginine, apoE-4 no cysteine and 2 arginines. This affects the affinity of the lipoprotein particles that contain them for specific receptors in both the liver and extrahepatic receptors. Homozygotes having apoE-2/2 are characterized by reduced clearance of VLDL and chylomicron residues from the bloodstream through the liver because apoE-2 binds poorly to the apoE receptor. In addition, individuals with apoE-2 have reduced lipolytic conversion of VLDL to LDL, so they have less LDL and more VLDL in plasma. They develop so-called dysbetalipoproteinemia (Type III according to Fredrickson). Individuals with apoE-4 are characterized by increased conversion of VLDL to LDL, which leads to a decrease in plasma VLDL and, conversely, to an increase in LDL.

Lipoprotein Lp (a)

Elevated serum concentrations of the specific lipoprotein Lp (a) are considered an independent factor. It is a lipoprotein class with a molecular weight greater than 5.4 million, moving on 1-region electrophoresis; in ultracentrifugation, it is found in the HDL-fraction and is referred to as "sinking pre-". The major apolipoprotein is apo B100; However, Lp (a) still has a specific antigen: apoprotein (a) = apo (a). Apo (a) is composed of 7 "kringle" domains that have high homology to the "kringle" domains of plasminogen, as well as 1 protease domain. The similarity with plasminogen leads to the possibility of occupying receptor sites on fibrin and to inhibiting fibrinolysis; Thus, Lp (a) has a double risk effect: it is atherogenic (presence of apo B-100) and antifibrinolytically [presence of apo (a)]. Apo (a) has 6 genetically determined isoforms: F, B, S1, S2, S3, S4, which differ in molecular weight; however, 11 other polymorphic forms have been described. Apo (a) is metabolized differently than other apoB-containing lipoproteins. It can be considered as an acute phase reactant because it temporarily increases e.g. after major surgery or acute myocardial infarction. A transient increase was also observed in unstable angina pectoris (without an increase in CRP). The physiological function is unknown. It is speculated that its ability to bind to fibrin allows the delivery of cholesterol molecules to the organizing thrombus.

Physiological values of Lp (a) (adults): 0.10–0.2 g / l

Risk value:> 0.30 g / l

Note: The level of the whole Lp (a) molecule may not correspond to the degree of risk of atherosclerosis (due to different genetic variants). The determination of "free" apolipoprotein (a) is of greater significance. The binding of Apo (a) to the LDL particle occurs extracellularly so that both complete Lp (a) and free Apo (a) are found in the bloodstream.

LDL-cholesterol (calculated) (LDL-C)

The Planell calculation, which also includes the ApoB determination, has a better explanatory value than the Friedewald formula. LDL-C (mmol / l) = 0.41. total. cholesterol (mmol / l) - 0.32. triacylglycerols (mmol / l) + 1.70. ApoB (g / l) - 0.27

Tab. 3: Evaluation of cholesterolemia

Normolipidemic	Type IIa	Type IIb	Type IV
3,19±0,56	6,46±2,21	5,27±0,93	3,40±0,48

(It is particularly suitable for distinguishing Fredrikson type IIb from type IV(”cut-off”=4, 13 mmol/l)

Tab. 3: Increase in lipids and lipoproteins in relation to the risk of atherosclerosis (according to Assmann)

Parameter (mmol/l)	No risk	Suspicious range (need for treatment according to clinical finding)	High risk (must be treated)
S-triacylglycerols	< 1,7	1,7–2,3	> 2,3
S-cholesterol	< 5,7	5,7–6,7	> 6,7
S-LDL-cholesterol	< 3,9	3,9–4,9	> 4,9
S-HDL-cholesterol men	> 1,4	0,9–1,4	< 0,9
S-HDL-cholesterol women	> 1,7	1,2–1,7	< 1,2

Tab. 3: S-cholesterol values (in mmol / l) as a risk factor in different age groups (according to NIH)

Age group	Medium risk	High risk
2–19	> 4,4	> 4,78
20–29	> 5,17	> 5,7
30–39	> 5,7	> 6,2
40 a více	> 6,2	> 6,72

Tab. 3: Values of risk factors (according to Roseneu and van Biervliet)

Parameter	Infants	Adults
S-cholesterol (mmol/l)	> 4,13	> 6,2
S-HDL-cholesterol (mmol/l)	< 1,16	< 1,16
apo B (g/l)	> 0,90	> 1,10
apo A-1 (g/l)	< 1,10	< 1,10
apo A-I/apo B	< 1,2	< 1,0

Non-lipoprotein biochemical risk factors

Homocysteine

Homocysteine is an important (central) metabolite of methionine metabolism. It is not found in the diet but is formed from methionine during its metabolism to S-adenosylmethionine. Homocysteine can then be metabolized in four possible ways: In the so-called remethylation pathway, it obtains a CH3 group from betaine or

5-methyltetrahydrofolate to form methionine. The one with ATP gives S-adenosylmethionine, which is the immediate donor of methyl groups e.g. for purine core synthesis. In the transsulfuration pathway (i.e., when there is an excess of methionine or when cysteine is to be synthesized), homocysteine condenses with serine to form cystathionine, which hydrolyzes to ketobutyrate and cysteine. The fourth pathway is the export of intracellular homocysteine to the extracellular environment (when production outweighs utilization in the cell). About 1.2 mmol enters the plasma from the cells within 24 hours. An increase in both homocysteine free (about 5-10%) and bound (to albumin) and also as homo-cysteinyl cysteine was observed in vascular diseases. An increase in plasma homocysteine appears to be a separate risk (approximately 3-fold), especially for peripheral vascular diseases and cerebrovascular diseases, less so for coronary artery disease.

An inherited defect in homocysteine metabolism enzymes, such as cystathionine synthase or 10-methylene tetrahydrofolate reductase, leads to an increase in homocysteine. Similarly, deficiencies in some vitamins such as folic acid, vitamin B12 and pyridoxal phosphate (a derivative of vitamin B6) cause hyperhomocysteinuria. Smoking and drinking coffee also encourage her.

The pathogenesis of homocysteine-induced vascular damage is unclear. Homocysteine can impair endothelial cell function, even leading to endothelial cell damage; it also induces increased blood clotting. It affects the normal prothrombolytic and anticoagulant activity of endothelial cells. Physiological values: 11.58 ± 4.48 µmol / l (10.2–14.8 µmol / l) (12–15 µmol / l) (values increase with increasing age). Pathological increase (in µmol / l):

- slight increase 16-31
- medium increase 32–100
- significant increase .....> 100
- *patients with coronary artery bypass grafting (Hyánek, 1996) 14.2 ± 4.9 (women), 16.0 ± 5.3 (men)*
- *stroke: 15.7 ± 5.0*

This can be caused by:

- hereditary enzyme defect:

* heterozygous cystathionine-β-synthase deficiency (incidence 1-2%)
* decreased methylenetetrahydrofolate reductase activity
* reduced methyltetrahydrofolate-homocysteine-methyltransferase activity
* defects in the regulation of homocysteine metabolism by conversion to S-adenosylmethionine

Increase in other pathological conditions:

- classic homocystinuria (type I) (cystathionine-β-reductase deficiency): 258 µmol / l (and more) (Type II: methylcobalamin defect; type III: methylenetetrahydrofolate reductase deficiency)
- vitamin B12 deficiency
- folic acid deficiency
- other (psoriasis, leukemia, solid tumors, hyperthyroidism)
- increased creatine production
- decreased renal function

Elevated homocysteine is an independent risk factor for premature cardiovascular disease (risk increase of 20-30%).

The level of homocysteine is reduced by the intake of vitamins (folic acid, vitamin B12, pyridoxine), as well as increased consumption of vegetables and fruits. Therefore, in some cases of hyperhomocysteinemia, folate supplementation helps (5 mg / day; cave: epilepsy).

Note: It is very important for the determination to separate the plasma from the blood cells or the serum from the clot as soon as possible, preferably to take in ice-cooled samples and thus quickly transported to the laboratory for centrifugation (within 1 hour at the latest). Otherwise, there is a significant artificial increase.

Stress test with L-methionine (according to Hyánek)

Principle: after administration of L-methionine (7 g) its increase is monitored in 6 hours. A more significant increase indicates a deficit of dihydrofolate reductase activity and the risk of vascular endothelial damage by homocysteine.

Fibrinogen

Elevated plasma lipoprotein poses another potential risk for coronary heart disease.

Tissue plasminogen activator (tPA)

Represents another possible risk factor for myocardial infarction (P. Ridker) Values:

- control: 9.2 g / l
- high risk: over 12.2 g / l (triple risk)
- low risk: below 5.2 g / l

Microalbuminuria

Microalbuminuria is defined as abnormal urinary albumin excretion at between 20-200 /g / min (ie 30-300g / day). It is associated with a number of cardiovascular risk factors such as:

- increased blood pressure and altered daily blood pressure profile
- insulin resistance and sensitivity to NaCl
- atherogenic lipid profile
- systemic endothelial dysfunction
- increased activity of the renin-angiotensin system

Microalbuminuria is a marker of early organ damage in essential hypertension such as left ventricular hypertrophy, retinal vessel damage, thickened carotid wall, and glomerular hyperfiltration. Examination of microalbuminuria and its monitoring is therefore a valuable and relatively inexpensive laboratory marker (predictor of morbidity and mortality) of cardiovascular diseases.

Reaven Multiple Metabolic Syndrome (= "Syndrome X")

It is an association of several risk factors, probably based on insulin resistance associated with obesity, hypertension, hypertriacylglycerolemia, hyperglycemia, which were added by others such as hyperuricemia, hirsutism, blood clotting and fibrinolysis disorders, microalbuminuria and the formation of so-called small; Importantly, all of these signs are associated with the development of premature atherosclerosis. However, the metabolic syndrome and its causes cannot be understood as a manifestation of wear and tear or ageing, but it is based on genetically modified terrain

Leptin

Obesity is a risk factor for many diseases of civilization. Leptin is a proteohormone of Mr = 16,000 belonging to the family of hematopoietic cytokines, which is a product of the OB gene on chromosome 7q31.3 and which plays a key role in the regulation of body weight. It is produced by differentiated adipocytes. The main factor determining the level of circulating leptin is the amount of adipose tissue. Concentration increases with body mass index BMI =

[weight (in kg)] / [height (in m)] 2 or with body fat content. Even small variations in body fat result in significant differences in leptin levels - from 0.03 g / l in anorexic patients to 100 g / l in extremely obese individuals. Leptin levels depend on age (up to 20 years).

The biological effect of leptin is mediated by the leptin receptor (OB-R), which belongs to the class I family of cytokine receptors. Leptin causes a reduction in food intake (in experimental animals) and increased energy expenditure, including thermogenesis. In addition, leptin affects a number of endocrine systems. This effect is mediated by the action on the hypothalamus, namely the production of neuropeptide Y (NPY) - leptin suppresses the expression and secretion of NPY, which is a stimulator of food intake and regulates a number of pituitary hormones. In very simple terms, leptin is a signal from adipose tissue that informs the body of the energy stores stored in fat depots. (Blum, 1997).

Diseases and conditions associated with secondary hyperlipoproteinemia

Genetically determined primary hyperlipoproteinemia must be distinguished from conditions in which hyperlipoproteinemia may occur secondarily. Elevated lipid levels usually disappear when the underlying disease is corrected. They represent about 40% of all hyperlipoproteinemias. Their treatment consists mainly in the treatment of the primary disease. These include hyperlipoproteinemia in the following conditions:

Obesity

About 30-50% of patients with obesity also have hyperlipoproteinemia characterized by biochemical changes as in type IV. These disappear after treatment with a low-energy diet and after a ban on alcohol.

Alcoholism

In some "predisposed" patients, even mild but regular alcohol consumption induces changes in the lipid spectrum corresponding to type IV (excessive VLDL production for acyl-CoA accumulation). In chronic alcoholics, the condition is exacerbated and there is not only hyper-VLDLemia but also hyperchylomicronemia (lipid profile as in type V). At the same time, there is a risk of acute pancreatitis.

In Zieve's syndrome, which can be found in chronic, malnourished alcoholics, hypertriacylglycerolemia is accompanied by liver dysfunction with jaundice and hemolytic anemia.

Hepatopathy

Acute hepatitis, chronic hepatitis and acute liver failure are characterized by a marked increase in triacylglycerol at normal or reduced cholesterol levels. In acute hepatitis, the lipid profile corresponds mostly to type IV, in chronic hepatitis rather to type IIb. The process is conditioned by the synthesis of an abnormal LDL-fraction called lipoprotein X (LP-X), which occurs especially in cases with cholestasis. Elevated triacylglycerols are usually associated with decreased hepatic LCAT production. In cases of liver cirrhosis with higher levels of non-esterified fatty acids but with normal LCAT activity, plasma triacylglycerols are normal. LCAT activity also correlates with cholesterol ester levels; their reduction, which is typical for diffuse hepatocellular damage, is due to the low activity of LCAT. In hepatocellular carcinoma, about a quarter of adult patients has hypercholesterolemia. Hypercholesterolemia (increased LDL) is also common in acute intermittent porphyria.

Cholestasis

In both intrahepatic and extrahepatic cholestasis, there is marked hypercholesterolemia (increase 2–5 times), especially an increase in "free" cholesterol. LP-X-lipoprotein has been shown to be a sensitive indicator of cholestasis in serum (unlike other lipoproteins, it travels to the cathode in an agar gel ELFO). Except for cases of biliary cirrhosis and hepatocellular carcinoma, LP-X levels are higher in extrahepatic obstruction than in intrahepatic obstruction.

Diabetes mellitus

In 40% of diabetics, hyperlipoproteinemia is type IV; type IIb is less common and type V is rare. Classical "diabetic hyperlipemia", ie mainly an increase in VLDL (triacylglycerols: 11, 3–20 mmol / l, occurring under the image of severe mixed hyperlipoproteinemia with eruptive xanthomas and lipaemia retinalis and manifestations of ketosis, is found only in untreated type I diabetics (insulin-independent) Insulin deficiency leads to the mobilization of triacylglycerol in adipose tissue, excessive amounts of released fatty acids are metabolized in the liver to ketone bodies and part to triacylglycerol, which enters VLDL. In both cases, this leads to hyper-VLDL.

Nephropathy

Nephrotic syndrome (regardless of its etiology) is characterized by severe hypercholesterolemia. The increase in triacylglycerols is variable. In milder forms, hyperlipidemia is type IIa, in more severe ones it is type IIb. That is, mainly the increase in LDL, which increases in proportion to the decreasing albumin level. When albumin drops below 10 g / l, VLDL also increases, sometimes extremely (with a corresponding increase in triacylglycerols). VLDL in nephrotic syndrome is rich in cholesterol esters. The mechanism of hyperlipoproteinemia in nephrotic syndrome is not entirely clear; perhaps it is the adaptive proteosynthesis of plasma proteins (and therefore lipoproteins) to significant urinary protein loss in order to maintain circulatory oncotic pressure. The incidence of myocardial infarction in adult patients is increased. In patients with chronic renal failure (approximately 70%), there is type IV hyperlipoproteinemia with decreased HDL. Type II a or IIb hyperlipoproteinemia occurs in 90% of renal transplant patients.

Endocrinopathy

They are very often associated with disorders in lipid metabolism.

Hypothyroidism

In hypothyroidism, there is almost always hypercholesterolemia (type IIa or IIb) with increased LDL and HDL. VLDLs tend to be normal. The catabolism of apoprotein B is reduced, thus disrupting the conversion of "VLDL-remnants".

Steroid hyperlipoproteinemia

Hypercholesterolemia and hypertriacylglycerolemia are often present when glucogenic corticoids or Cushing's syndrome are administered (cholesterol elevations always predominate). Both VLDL and LDL (endogenous or mixed hyperlipoproteinemia) are elevated; type IIb according to Fredrickson's scheme.

Estrogenic hyperlipoproteinemia

Estrogens are known to increase HDL levels (premenopausal period in women), which is attributed to the antiatherogenic protection of women (unlike men). Estrogen administration (eg in the form of birth control pills) increases VLDL, especially in combination with nortestosterone derivatives.

Hypopituitarism

Hyperlipoproteinemia (increased triacylglycerols, less increased cholesterol) often occurs in hypopituitarism. Growth hormone deficiency leads to reduced fatty acid oxidation in the liver and ketogenesis with concomitant increased synthesis of triacylglycerols and VLDL.

Acromegaly

The level of triacylglycerols and cholesterol is highly variable. The mild form is associated with a slight increase in triacylglycerols and a slight decrease in cholesterol. Insulin resistance is usually increased.

Stress hyperlipoproteinemia

Stressful situations are accompanied by the mobilization of non-esterifying fatty acids from adipose tissue. Elevated levels of triacylglycerols (endogenous hypertriacylglycerolemia) are caused by both increased secretion of VLDL from the liver and impaired catabolism. Cholesterol and LDL levels are reduced. Stress hyperlipoproteinemia occurs in conditions such as acute myocardial infarction, spontaneous or emotional stress, extensive burns, sepsis-induced by particularly gram-negative flora.

Anorexia nervosa

About half of the patients develop hypercholesterolemia; triacylglycerol levels are usually normal. Perhaps this is due to reduced faecal excretion of cholesterol metabolites and limited transport of cholesterol to the liver.

Pheochromocytoma

Sometimes there is a type IV hyperlipoproteinemia.

Iatrogenic hyperlipoproteinemia

Administration of some drugs may induce hyperlipoproteinemia:

- thiazide preparations increase mainly VLDL (type IV),
- corticosteroids cause long-term hyperlipoproteinemia type IV, at high doses type I,
- blockers (propranolol) sometimes cause hyper-VLDLemia (type IV).

Exogenous hypercholesterolemia

Excessive cholesterol in the diet leads to hypercholesterolemia. A case was reported of a patient who ate 8-12 egg yolks (about 3.5 g of cholesterol) on a regular basis. Her cholesterol level was around 24 mmol / l. During a normal diet, the level gradually decreased.

Monoclonal gammopathy

Endogenous hyperlipoproteinemia (VLDL remnants) may be found in patients with paraproteinemia. However, hypocholesterolemia (LDL reduction) is also common in IgA myeloma. There are also complexes of VLDL and LDL with abnormal immunoglobulins. Clinical manifestations of hyperlipoproteinemias in paraproteinemias are usually palm xanthomas (characteristic).

Glycogenosis

Endogenous or mixed hyperlipoproteinemia is characteristic of hepatorenal glycogenosis (Gierke's disease). It is probably caused by hypoglycaemia, which leads to hyperinsulinism and increased fat breakdown from adipose tissue. Therefore, treatment consists in preventing hypoglycemic conditions by feeding more frequently. There may be hyperlipoproteinemia in other hepatic glycogenosis (type III and type IV).

Hyperuricemia

It is often associated with type IV hyperlipoproteinemia.

Lipid storage disorders

In addition to disorders of lipid metabolism, characterized mainly by changes in circulating lipoproteins, we find disorders whose place lies in the conversion of lipids in cells (enzyme defects in lysosomes). We can divide them into metabolic disorders of cholesterol catabolism and disorders in the conversion of sphingolipids.

Cholesterol storage disorders

Wolman's disease

It is a rare inherited metabolic disorder with the autosomal recessive transmission, in which cholesterol and triacylglycerol esters are deposited in the cells of the liver, kidney, adrenal gland, hematopoietic system and small intestine. This is due to the lack of lysosomal acid lipase. The disease manifests itself only a few weeks after birth (at six months): failure to thrive, hepatosplenomegaly, recurrent vomiting, persistent diarrhoea with steatorrhea, bilateral adrenal calcification. The course is usually fatal. Confirmation of the diagnosis is histochemical (lysosomal acid lipase deficiency, accumulation of cholesterol esters in the lysosomes of affected tissue cells).

Cholesterol ester storage disease

It's a milder equivalent of Wolman's disease. Acid lysosomal lipase deficiency is incomplete (activity 1–20% of normal); clinical manifestations appear much later (patients live to be 40 years old), hepatomegaly and the extent of cholesterol ester storage in cells is not so great. Both diseases are thought to be allelic mutations affecting the same genetic locus.

Familial lecithin: cholesterol acyltransferase (LCAT) deficiency

It is a deficiency of a key enzyme that performs cholesterol esterification. It is a very rare inherited disorder with the autosomal recessive transmission. Serum triacylglycerols are elevated and cholesterol levels are variable; but cholesterol esters are missing (3-30% vs. 75-70%). Lipids are deposited on the cornea (milky clouding), in the glomerular membrane (proteinuria), in the bone marrow and spleen (see blue histiocytes), in erythrocytes (anemia), in the vascular wall (atheromas). There are also changes in plasma lipoproteins: triacylglycerolemia 2.26–11.3 mmol / l. Most lipoprotein classes are abnormal (different sizes, different ELFO motility, etc.).

Sphingolipidosis

It is a group of inherited disorders of membrane lipid metabolism, namely sphingolipids, which are manifested by the accumulation of these lipids in the relevant organs. Their schematic overview is given in the table.

Tab. An overview of the most important sphingolipidoses

Name	Clinical manifestations	Place of damage	Enzyme defect
Gangliosidosis (Norman-Landig disease)	mental retardation, degeneration of the nervous system, hepatosplenomegaly, cherry red macula on the ocular background	brain, liver, spleen, bones	ganglioside-β-galactosidase
Tay-Sachs disease disease	mental retardation, degeneration of the nervous system	brain, nervous system	hexosaminidase A
Glucocerebrosidosis (Gaucher disease - 3 types)	mental retardation, degeneration of the nervous system, hepatosplenomealia, erosion of the cortex of the long bones and pelvis (pathological fractures)	liver, spleen, nervous system, bones cerebrosyl	β-glucosidase
Galactosylceramidosis (Krabbe disease)	mental retardation, degeneration of the central and peripheral nervous system (globoid bodies)	brain, nervous system	cerebrosyl β-galactosidase
Galactosylceramidosis (Scholz 's disease)	mental retardation, degeneration of the central and peripheral nervous system	brain, nervous system	arylsulfatase A
Ceramide trihexosidosis (Fabry disease)	diffuse angiokeratoma, corneal damage	blood vessels, skin, kidney	α-galaktosidase A
Sphingomyelinosis (Niemann-Pick disease, 5 forms: A to E)	hepatosplenomegaly, mental retardation, degeneration of the nervous system, cherry red macula on the ocular background, "foam" cells in the bone marrow	liver, spleen, brain, bone marrow	sfingomyelinase
Ceramidosis (Farber's disease)	mental retardation, degeneration of the nervous system	skin, joints, brain	ceramidase

References

Links

Related articles

- Lipid metabolism disorders (general)
- Lipoproteins
- Lipoproteins (clinic)
- Hypolipidemic treatment
- Atherosclerosis
- Obesity

Resources

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